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09/584,328	05/30/2000	Kurt E. Petersen	22660-0026US	1737

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EXAMINER

QUAN, ELIZABETH S

ART UNIT	PAPER NUMBER
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1743

DATE MAILED: 02/27/2003

#24

Please find below and/or attached an Office communication concerning this application or proceeding.

Remail of paper #11

Office Action Summary

Application No.

09/584,328

Applicant(s)

PETERSEN ET AL.

Examiner

Elizabeth Quan

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 22-42 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 22, 24, 28, 29 and 34-42 is/are rejected.
- 7) ☒ Claim(s) 23, 25-27 and 30-33 is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: .

DETAILED ACTION

Claim Objections

1. Claim 33 is objected to because of the following informalities: Claim 33 depends on objected claim 1. Appropriate correction is required.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

3. Claim 30, 35 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. Claim 30 recites the limitation "the sample flow path" in the second line. There is insufficient antecedent basis for this limitation in the claim.

5. Referring to claim 35, it is unclear whether the first and second sheets are the same as the polymeric film. If they are not the same, what is the relationship between the sheets and the film? Is the sheet superimposed upon the film or vice versa?

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claim 22 is rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,580,523 to Bard.

Referring to claim 22, Bard discloses a device for conducting a chemical reaction (see ABSTRACT). The device comprises of a body (20) and a reaction vessel (100) (see FIGS. 1-3; COL. 5, lines 19-48; COL. 6, lines 26-33). The body (20) has a first channel (50) and second channel (51) formed therein (see FIGS. 1-3; COL. 5, lines 19-48; COL. 6, lines 26-33). The reaction vessel (100), which extends from the body (20), includes a reaction chamber with an inlet port connected to the reaction chamber via an inlet channel and outlet port connected to the reaction chamber via an outlet channel (see FIGS. 1-3; COL. 5, lines 19-48; COL. 6, lines 26-33). The inlet port of the reaction vessel (100) is connected to the first channel (50) in the body (20), and the outlet port of the reaction vessel (100) is connected to the second channel (51) in the body (20) (see FIGS. 1-3; COL. 5, lines 19-48; COL. 6, lines 26-33). Therefore, Bard includes all the limitations in claim 22.

8. Claims 22, 24, and 29 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,498,392 to Wilding et al.

Referring to claims 22, 24, and 29, Wilding et al. disclose a device for conducting a chemical reaction (see ABSTRACT). The device comprises of a body (50) and a reaction vessel (10) (see FIGS. 1-18). Applying the Merriam-Webster Collegiate Dictionary definition of extend, which is to cause to be of greater area or volume, the reaction vessel (10) extends from the body (50) (see FIGS. 1-18). The reaction vessel (10) includes a reaction and/or mixing chambers (22A, 22B, or 22C) with an inlet port (16A, 16B, 16C, or 16D) connected to the reaction and/or mixing chambers (22A, 22B, or 22C) via an inlet channel and outlet port (16A, 16B, 16C, or 16D) connected to the

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reaction chamber via an outlet channel (see FIGS. 1-18; COL. 8, lines 50-67; COL. 9, lines 51-67; COL. 10, lines 11). The inlet port (16A, 16B, 16C, or 16D) of the reaction vessel (10) is connected to the first channel (56) in the body (50), and the outlet port (16A, 16B, 16C, or 16D) is connected to the second channel (59) in the body (50) (see FIGS. 1-18; COL. 8, lines 50-67; COL. 9, lines 51-67; COL. 10, lines 11). A pump (52) is used to force fluid in the first channel (56) in the body (50) to flow through the inlet port (16A, 16B, 16C, or 16D) of the reaction vessel (10) and into the reaction chamber (22) (see FIGS 1-18; COL. 8, lines 65-67). Therefore, Wilding et al. include all the limitations in claims 22, 24, and 29.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35

U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

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11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claim 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,580,523 to Bard or U.S. Patent No. 5,498,392 to Wilding et al.

Referring to claim 28, neither Bard nor Wilding et al. quantify the width and thickness of the chamber. Applying the decision of *In re Aller*, discovering the optimum workable range of the width and thickness of the chamber involves only routine skill in the art. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to determine through experimentation a width to thickness ratio of 4:1 and a thickness range of 0.5 to 2 mm to maximize sensitivity and precision of the detection device using a light source and provide an optimal size chamber for creating a certain amount of product.

13. Claims 34-37 and 39-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,674,743 to Ulmer in view of U.S. Patent No. 5,863,502 to Southgate et al.

Referring to claims 34-37 and 39-42, Ulmer discloses an apparatus for automated DNA sequencing, which comprises a cleaving station (50), transport system (70), and detection station (90) (see ABSTRACT; FIG. 7; COL. 16, lines 14-16).

Cells are introduced into sample chamber (52) consisting of a small depression in a substrate at the edge of a transparent cover plate (see FIG. 7; COL. 19, lines 14-16). Cells may be monitored by the microscope system equipped with an infrared single-beam gradient optical trap (see COL. 19, lines 25-27). The microchannels may have electrodes for providing an electric field to the sample fluid, which causes the cells to migrate single-file into the exit capillary channel (53) (see COL. 19, lines 56-61). The target cell for sequencing is identified by visual inspection using the microscope (65), and the target cell is confined in the optical trap and translated along the exit channel (53) to the cell isolation chamber (56) (see COL. 19, lines 63 and 64; COL. 20, lines 2-4). A bifurcation (54) in the capillary channel allows for sorting or selection of specific cells for sequencing via diverting a cell into one branch or the other of the capillary channel by applying an electric field along the selected branch (see COL. 20, lines 7-14). With the isolation of a target cell in chamber (56), an appropriate culture medium to replicate DNA to the point of metaphase is introduced into the chamber through another microchannel (57) (see COL. 20, lines 25-32). Subsequently, cells may be lysed through chemical and/or physical techniques (see COL. 20, lines 45-51). When the cell has been disrupted and the chromosomes are released, the chromosomes are separated into individual compartments (see COL. 21, lines 9-11). Individual chromosomes are captured and transported in microchannel (58) to isolation chamber (60) via a single-beam gradient optical trap (see COL. 21, lines 9-16). The DNA is confined in an extended conformation in a narrower capillary channel (62) with the end of the DNA distal from the exonuclease binding site is immobilized on a microscopic bead (68) and

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the other end with a single bound molecule of exonuclease (67) positioned at the mouth of microchannel (72) at the nozzle (80) (see COL. 22, lines 56-61; COL. 30, lines 27-33). Nucleotides (64) are cleaved from DNA strand (66) at the nozzle (80) in microchannel (72), and the nucleotides are detected by detection station (90) (see COL. 30, lines 34-36).

A flow cell (500), which has a nozzle (72) and heating element (73) adapted to mate with the opening of microchannel (75), extends from the micromachined body of the cleaving station (50), incorporates elements of the transport system (70), and provides access to the nucleotide-containing matrix (88) for the detection and identification at the detection station (90) (see FIGS. 7-12 and 15; COL. 16, lines 36-39; COL. 32, lines 54-58; COL. 33, lines 27-29). Flow cell (500) comprises three sheets (510,520,530) made of glass, which has a certain degree of rigidity or flexibility (see FIG. 15; COL. 33, lines 6 and 7). Sheets (510,530) form major walls sandwiching sheet (520) with connecting sidewalls angularly offset from each other by about 90 degrees (see FIG. 15). Microchannel (76) is disposed in the lower two sheets (520,530), wherein the upper half of the channel is in sheet (520) and the lower half of the channel is in sheet (530) (see FIG. 15; COL. 33, lines 23-25). Sheath fluid (77) enters microchannel (76) at port (78) at constant laminar flow rate (see COL. 31, lines 39 and 40). Microchannel (75) is formed in sheet (530) (see FIGS. 7 and 15; COL. 33, lines 62-64). A nucleotide stream enters the center of a coaxial sheath solution in the same direction in microchannel (75) through nozzle (80) (see COL. 17, lines 1-3).

Radiation from a radiation source (92) is directed to matrix (88) in microchannel (76) in the bottom of sheet (530) by external lens, which also collects the fluorescent emission from individual nucleotides (64) in matrix (88) for detection by detection system (94) (see FIGS. 7-12 and 15; COL. 33, lines 34-38; COL. 37, lines 49-64; COL. 39, lines 42-55). Optical access to matrix (88) may also be provided on the upper surface of the flow cell (500) by imaging through the glass refrigerator (510) and upper sheet of the flow channel (520) or through sheets (520,530) by one or more waveguides (95) defined in the sheets (see FIGS. 7-12 and 15; COL. 33, lines 39-44). The entire flow cell (500) is contained within a stainless steel vacuum dewar to thermally isolate the flow cell (500) from the ambient environment (see COL. 33, lines 45-49). The dewar has optical windows positioned over the flow cell (500) to provide optical access for fluorescence detection of nucleotides (64) and manipulation of the DNA molecule (66) by an optical trap (69) operating on the optical handle (69) (see COL. 33, lines 49-54).

The upper sheet (510) contains a refrigeration system (85), which comprises a gas inlet (511), gas outlet (512), countercurrent heat exchanger (514), expansion capillary (516), and reservoir (518) (see FIG. 15; COL. 33, lines 7-11). For a cooling effect a high pressure gas is supplied to inlet (511) which goes through the countercurrent heat exchanger (514) to the expansion capillary (516), where it expands and cools (see FIG. 15, COL. 33, lines 13-16). The gas enters reservoir (518) and the cooled vapor reenters the heat exchanger (514) to outlet (512), precooling incoming gas (see FIG. 15; COL. 33, lines 16-18). The refrigeration system is operated in an open cycle with the pressurized gas supplied by a high pressure tank and provides a steep temperature gradient between

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the nozzle (80) and point of fluorescence excitation in the detection (90) (see COL. 32, lines 38-42; COL. 33, lines 20-22).

Ulmer does not disclose that the sheets are polymeric. However, Southgate et al. disclose three flexible films (110A, 110B, 110C) preferably constructed of polyethylene, polyvinylidene fluoride, or polyethylene/polyethylene terephthalate bilayer film (see COL. 11, lines 47-58). The films cover and seal the chambers and channels, such that the film can hold in the liquids. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device of Ulmer to use polymeric films as in Southgate et al. to cover and seal the chambers and channels, such that the film can hold in the liquids.

14. Claim 38 is rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,674,743 to Ulmer in view of U.S. Patent No. 5,863,502 to Southgate et al.

Referring to claims 5 and 16, Ulmer in view of Southgate disclose a dewar containing a flow cell (500) provided with optical access for purposes of fluorescence detection of nucleotides (64) and manipulation of the DNA molecule (66) by an optical trap (69) operating on the optical handle (68) (see COL. 33, lines 49-54). To maximize the light collection efficiency of the objective lens, a high numerical aperture is desired (see COL. 33, lines 54 and 55). Minimizing the working distance between the objective lens and the matrix (88) is also desired and may be accomplished by using a minimal thickness window in the vacuum dewar, minimizing the vacuum gap between the inside surface of the window and the surface of the flow cell (500), and minimizing the thickness of the sheet (530) along with the depth of its microchannel (76) (see COL. 33,

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lines 49-64). Ulmer in view of Southgate et al. do not quantify the width and thickness of the flow cell (500). Applying the decision of *In re Aller*, discovering the optimum workable range of the width and thickness of the chamber involves only routine skill in the art. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to determine through experimentation a width to thickness ratio of 4:1 and a thickness range of 0.5 to 2 mm to maximize the light collection efficiency of the objective lens and minimize the working distance between the objective lens and matrix to achieve greater sensitivity.

Allowable Subject Matter

15. Claims 23, 25-27, 30-33 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

16. The following is a statement of reasons for the indication of allowable subject matter: The prior art of record does not teach or suggest a reaction vessel extending from the body in combination with the limitations in the base claim, specifically the structural relationships and connections of the channels in the body and reaction vessel.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Quan whose telephone number is (703) 305-1947. The examiner can normally be reached on M-F (8:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on (703) 308-4037. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 879-9310 for regular communications and (703) 872-9311 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0661.

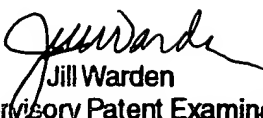
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Elizabeth Quan
Examiner
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